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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/373,018	08/11/1999	HUW M. NASH	10845/014002	2132

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EXAMINER	
MORAN, MARJORIE A	
ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 02/10/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/373,018	NASH ET AL.	
	Examiner	Art Unit	
	Marjorie A. Moran	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 April 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *16-22 and 54-63* is/are pending in the application.

4a) Of the above claim(s) *54-63* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *25 November 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Election/Restrictions

Claims 54-63 are again withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected Invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 15.

An action on the merits of elected claims 16-22 follows. All rejections and objections not repeated below are hereby withdrawn,

Drawings

The corrected or substitute drawings were received on 11/25/02. These drawings are acceptable to the examiner.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 16, 19-20, and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over HSIEH et al. (IDS ref; Molec. Diversity (1996) vol. 2, pages 189-196) in view of CARRELL (IDS ref : Chemistry and Biology (1995) vol. 2 (3), pp. 171-183).

Applicant's arguments with respect to claims 16, 19-20 and 22 have been considered but are moot in view of the new ground(s) of rejection.

Claim 16 recites a method of identifying a member of a mass coded combinatorial library which is a ligand for a first biomolecule wherein the biomolecule is contacted with the library and a complex allowed to form, unbound members of the library are separated from the complex, the complex dissociated, and the identity of the dissociated members of the library (i.e. ligands) identified by determination of the molecular mass of each ligand. Claim 16 further limits the library to one comprising compounds of the general formula XY_n, wherein n=2-6, there are at least 250 distinct combinations of n peripheral moieties, and at least 90% of the combination of N peripheral moieties has a molecular mass sum different from all other combinations of moieties. Claim 19 limits the biomolecule to be comprised in a solution which is contacted with the library to form a solution comprising biomolecule-ligand complexes and unbound library members. Claim 20 limits the method of claim 19 to one wherein unbound members of the library are separated from biomolecule-ligand complexes with a size-exclusion chromatography column. Claim 22 limits the biomolecule to a protein.

HSIEH teaches identification of members of a small molecule library as ligands for target biomolecules, specifically proteins, by allowing complexes between the biomolecule and library members to form in solution, separating complexes from unbound library members by passing the mixture over a size-exclusion chromatography column, dissociating the complexes, and identifying the ligands by mass spectrometry (pp. 192 and 194-195). HSIEH specifically teaches that his library may be combinatorial and may comprise peptides (p. 190). HSIEH does

not teach that a library comprising compounds of the general formula XY_n, wherein n=2-6, there are at least 250 distinct combinations of n peripheral moieties, and at least 90% of the combination of N peripheral moieties has a molecular mass sum different from all other combinations of moieties.

CARREL teaches synthesis of a peptide combinatorial library for use in screening wherein building blocks for the library are chosen such that "nearly all" the compounds would possess a unique molecular weight (p. 173). CARRELL teaches that his core (scaffold) molecule may be a fused ring (p. 173, Fig. 3), teaches acyl chloride reactive groups on his core molecule (Fig. 3), and teaches reactive groups comprising amines (pp. 173-174). CARRELL teaches a library for screening which comprises over 50,000 *different* molecules (p. 176).

Although CARRELL does not specifically teach a library of at least 250 compounds (combinations) wherein at least 90% have a distinct molecular weight, the combined teachings of CARREL for various library sizes, and specifically for a library of over 50,000 different molecules and his teaching for using a computer program to choose "combinations" of building blocks to provide a library wherein "nearly all" the members have a unique molecular weight suggests a library with over 250 compounds wherein "nearly all", or over 90% have a distinct molecular weight/mass.

It would have been obvious to one of ordinary skill in the art to have used any of the peptide libraries of CARRELL for screening in the method of HSIEH where the motivation would have been to identify members of the library which are ligands/inhibitors of trypsin, as suggested by CARRELL's teaching for screening his library for trypsin inhibitors. One skilled in the art would reasonably have expected success in screening CARRELL's library using the method of HSIEH because both teach solution-based screening of peptide/ligand libraries for binding to a protein.

Claims 16, 19, and 20-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over BREEMAN et al. (IDS ref; Anal. Chem. (1997)) in view of CARRELL (IDS ref : Chemistry and Biology (1995) vol. 2 (3), pp. 171-183).

Applicant's arguments with respect to claims 16, 19, and 20-21 have been considered but are moot in view of the new ground(s) of rejection.

Claim 16 recites a method of identifying a member of a mass coded combinatorial library which is a ligand for a biomolecule, as set forth above. Claim 19 limits the method to one performed in solution phase, as set forth above. Claim 21 limits the method of claim 19 to one wherein unbound library members are separated from ligand-biomolecule complexes using a size-exclusion membrane.

BREEMAN teaches identification of members of a library which are ligands for an enzyme wherein the enzyme and library members are allowed to associate in solution in an ultrafiltration chamber, on one side of an ultrafiltration/size exclusion membrane, unbound library members are washed away (though the membrane), and bound members are dissociated from the enzyme and identified by mass spectrometry (p. 2163, left column). BREEMAN does not teach a library comprising at least 250 members wherein at least 90% of the members have distinct molecular mass sums.

CARRELL teaches and suggests a library wherein 90% of the members have distinct molecular mass sums, and wherein the library may comprise as many as 50,000 different members/combinations of moieties.

It would have been obvious to one of ordinary skill in the art to have used any of the peptide libraries of CARRELL for screening in the method of BREEMAN where the motivation would have been to identify members of the library which are ligands/inhibitors of trypsin, as

suggested by CARRELL's teaching for screening his library for trypsin inhibitors, and BREEMAN's method of screening for enzyme ligands. One skilled in the art would reasonably have expected success in screening CARRELL's library using the method of BREEMAN because both teach solution-based screening of peptide/ligand libraries for binding to a protein/enzyme.

Claims 17-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over HSIEH et al. (IDS ref; Molec. Diversity (1996) vol. 2, pages 189-196) in view of CARRELL (IDS ref : Chemistry and Biology (1995) vol. 2 (3), pp. 171-183) as applied to claims 16 and 21 above, and further in view of REBEK et al. (IDS ref; WO 9519359).

Applicant's arguments with respect to claims 16018 and 21 have been considered but are moot in view of the new ground(s) of rejection. In response to the argument that REBEK does not teach a mass-coded library comprising at least 250 combinations of moieties (compounds) wherein at least 90% of the members of the library have a distinct molecular weight, it is noted that REBEK is not relied upon for a teaching of a mass-coded library in the instant rejection, but is relied upon for his teaching that members of a combinatorial library which bind to a protein may be identified using a protein which is immobilized on a solid support, specifically in a chromatographic column. CARRELL is relied upon for teaching/suggesting a combinatorial library which meets the condition of the claims.

Claim 16 recites a method of identifying a member of a mass coded combinatorial library which is a ligand for a biomolecule, as set forth above. Claims 17-18 limit the biomolecule to be immobilized on a solid support, specifically a water-insoluble matrix in a chromatographic column.

HSIEH in view of CARRELL make obvious a method of identifying members of a library which are ligands for a protein, wherein the library comprises at least 250 compounds (combinations of moieties), and wherein each compound has a distinct molecular mass. HSIAH and CARRELL do not teach immobilization of their biomolecule (protein) on a solid support/matrix in a chromatographic column.

REBEK teaches a method of screening members of a library which are ligands of a protein wherein members of his library may bind to a protein which is immobilized on Sepharose in a column, teaches that nonbound members of the library may be washed away from bound members (ligand-biomolecule complexes), then dissociated and identified (p. 67).

It would have been obvious to one of ordinary skill in the art to have immobilized the protein in the method of HSIEH and CARRELL on Sepharose in a chromatographic column, as taught by REBEK, where the motivation would have been to facilitate iterative screening steps on the library with the same affinity column, as suggested by the iterative steps of CARRELL (pp. 177-179). One skilled in the art would reasonably have expected success in using an immobilized protein in the method of HSIEH and CARRELL because REBEK teaches that a library similar to that of CARRELL's may be successfully screened against a protein either in solution phase or immobilized on a column (pp. 67-68).

Conclusion

Claims 16-22 are rejected; claims 54-63 are withdrawn.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marjorie A. Moran whose telephone number is (703) 305-2363. The examiner can normally be reached on Monday to Friday, 7:30 am to 4 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on (703) 308-4028. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 872-9306 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 305-3524.

MARJORIE MORAN
PATENT EXAMINER

February 10, 2003